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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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FISH & NEAVE IP GROUP
ROPES & GRAY LLP
1251 AVENUE OF THE AMERICAS FL C3
NEW YORK, NY 10020-1105

EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 08/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/784,950	DAVIS ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,6,7,9-22 and 24-61* is/are pending in the application.

4a) Of the above claim(s) *11-21, 24, and 53-59* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,6,7,9,10,22,25-52,60 and 61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/30/01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-2, 4, 6-7, 9-22 and 24-61 are pending.

2. Applicant's election without traverse of Group I, claims 1-10, 22-23, 25-52 and 60-61 (now claims 1-2, 4, 6-7, 9-10, 22, 25-52 and 60-61) drawn to an isolated monoclonal antibody having an isotype that fixes complement and a variable region that binds to the epitope on CD147, method of making antibodies, a kit and a pharmaceutical composition and the heavy chain comprises the amino acid sequence of SEQ ID NO: 40 and the light chain comprises the amino acid sequence of SEQ ID NO: 41 as the species filed on 1/28/05, is acknowledged.

Upon reconsideration, the search has been extended to cover the heavy chain of SEQ ID NOs: 23, 25, 27, 29, 31, 33, 35, 37, and 39 and the light chain of SEQ ID NOs: 24, 26, 28, 30, 32, 34, 36, and 38.

3. Claims 11-21, 24 and 53-59 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

4. Claims 1-2, 4, 6-7, 9-10, 22, 25-52 and 60-61 are under examination as they read on an isolated monoclonal antibody having an isotype that fixes complement and a variable region that binds to the epitope on CD147, method of making antibodies, a kit and a pharmaceutical composition and the heavy chain comprises the amino acid sequence of SEQ ID NOs: 23, 25, 27, 29, 31, 33, 35, 37, 39 and 40 and the light chain comprises the amino acid sequence of SEQ ID NO: 24, 26, 28, 30, 32, 34, 36, 38 and 41 as the species.

5. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)).

6. The application claims benefit to international application No. PCT/US99/04583 filed on 03/03/1999. Applications that are filed on or after November 29, 2000, and that claim benefit to an earlier-filed international application must include in the first sentence of the specification an indication of whether the international application was published in English under PCT Article 21(2) (regardless of whether the benefit for such application is claimed in an application data sheet). See 37 CFR 1.78(a)(2). The indication, as required by 37 CFR 1.78(a)(2), is missing. Applicant must supply the missing indication as an amendment to the specification in the reply to this Office action.

7. The specification on page 1 should be amended to reflect the status of 09/124,758 and 09/034,607 and the relationship between 09/124,758 and 09/034,607and the instant application.

8. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because: Inventor Qiang Liu citizenship has been altered, a supplemental declaration identifying inventor Qiang Liu citizenship is required.
Further, inventor Alan R. Culwell residence and postal office address have been altered without being initialed and signed.

9. Formal drawing of Figure 2A is objected to because the Figure has a hand written insert that obscures the figure showings. Correction is required.

10. The specification is objected to for failing to provide a brief description of each individual Figure. Figure 2, 6, 7, 9, 15, 16, 19, 20 have panels labeled such as 2A and 2B which each individual panel must be separately described. Correction is required.

11. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

The specification on page 59, lines 16, contains a hyperlink. The attempt to incorporate subject matter into the patent application by reference to a hyperlink and/or other forms of browser-executable code is considered to be an improper incorporation by reference.

12. Applicant's IDS, filed 4/30/01, is acknowledged.

13. Claim 25 is objected to because they are dependent on a non-elected claim 24 and should be written as an independent claim.

14. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 1-2, 4, 6-7, 9-10, 22, 31 and 60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

I. The recitation "the antibody is not CBL1 (ATCC HB 8214)" recited in claims 1, 7, 10 and 22 is indefinite and ambiguous because the preamble of the said claims recites human monoclonal antibodies, while CBL1 (ATCC HB 8214) antibody is a murine IgM antibody. The claims are ambiguous because they are reciting a human monoclonal antibody but excluding a murine antibody.

II. The recitation "murine IgM, murine IgG2a, murine IgG2b, murine IgG3" recited in claims 4, 6, 9 and 10 is indefinite and ambiguous because it is unclear how a human monoclonal antibody would be a murine antibody.

III. The "kit" recited in claim 31 has no antecedent basis in base claim 31. Base claim 31 only recites an article of maufacture.

IV. Claim 60 is indefinite for being in improper Markush format. The Office recommends the use of the phrase "selected from the group consisting of ..." with the use of the conjunction "and" in listing the species. See MPEP 706.03(Y). The conjunction "and" is missing.

V. The recitation "similar to" recited in claim 10(b) is indefinite and ambiguous. The term "similar to" is relative term indicates that the binding against CEM cell lysates on Western bolt shares some qualities, but not identical. It is unclear which qualities are contemplated.

16. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

17. Claims 1-2, 4, 6-7, 9-10, 22, 28, 32, 35-40, 42, 45, 47-52: It is apparent that the CBL1 antibody which is also the starting material for ABX-CBL antibody is required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If they are not so obtainable or available, the enablement requirements of 35 U.S.C. 112, first paragraph, may be satisfied by a deposit of the pertinent hybridoma, which produce these antibodies. See 37 CFR 1.801-1.809.

In addition to the conditions under the Budapest Treaty, Applicant is required to satisfy that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a paten in U.S. paten applications.

It is noted that the specification on page 1 discloses that the CBL1 hybridoma has been deposited with the ATCC as HB 8214; however applicant has not provided objective evidence for the public availability of the CBL1/ATCC HB 8214 hybridoma.

However, it is noted that U.S Paten Nos. 5,330,896 and 5,643,740 claim this CBL1/ATCC HB 8214 hybridoma. Given these patented claims; it appears that the CBL1/ATCC HB 8214 antibody/hybridoma is publicly available.

18. Claims 1, 2, 4, 6, 7, 9, 10, 22, 27-29, 31-33, 35-36, 38-39 and 60-61 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated human monoclonal antibody having an isotype that fixes complement and a variable region that binds the epitope of SEQ ID NO: 1 (ITLRVRSH) on CD147 bound by the IgM monoclonal antibody ABX-ABL; a kit thereof, a pharmaceutical composition thereof and an article of manufacture thereof for the treatment of GVHD, and a human monoclonal antibody that binds to CD147 wherein the heavy chain and the light chain are 23 and 24, 25 and 26, 27 and 28, 29 and 30, 31 and 32, 33 and 34, 35 and 36, 37 and 38, 40 and 41, does not reasonably provide **enablement** for an isolated human monoclonal antibody having an isotype that fixes complement and a variable region that binds to the epitope on CD147 bound by the IgM monoclonal antibody ABX-CBL, "with the proviso that the antibody is not CBL1 (ATTCCHB 8214)" in claims 1, 7, 10, 22 , wherein the isotype is selected from the group consisting of "murine IgM, Murine IgG2a, murine IgG2b, murine IgG3" in claims 4, 6, 9, 10(c), cross-reacts with "hn-RNP-K protein", binds to a "consensus sequence on the CD147 comprising RVRS" in claim 10(e-f) or "to an epitope on CD147 comprising the consensus sequence RVRSH" in claim 22, a kit or an article of manufacture for the treatment of diseases having an etiology characterized by a "harmful presence of activated T cells, B cells, or monocytes" comprising a liquid preparation comprising an amount of an anti-CD147 antibody in pharmaceutically acceptable carrier and instructions on administering said preparation to a patient "suffering from any disease" "having the etiology characterized by a harmful presence of activated T cells, B cells, or monocytes" in claims 27, 31, 35, 38, or a human monoclonal antibody that binds to CD147 wherein the heavy chain has an amino acid sequence of SEQ ID NO: 23, 25, 27, 29, 31, 33, 35, 37, 39 and 40 in claim 60, or the light chain of SEQ ID NOs: 24, 26, 28, 30, 32, 34, 36, 38, and 41 in claim 61. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim.

The specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

Claims 1, 7, 10 and 22 recite that the human monoclonal antibody is not CBL1 (ATCC HB 8214). Since CBL1 (ATCC HB 8214) is a murine monoclonal antibody, it is clear to those skilled in the art that a human monoclonal antibody is not a murine monoclonal antibody by definition.

Claims 4, 6, 9 and 10 recites that the human monoclonal antibody having an isotype of murine

IgM, murine IgG2a, murine IgG2b, murine IgG3. Since the claimed antibody are human monoclonal antibodies, the specification is not enable for a human monoclonal antibody with an isotype of murine IgM, IgG2a, IgG2b, IgG3. It cannot be seen how a human monoclonal antibody would be a murine monoclonal antibody.

Claims 10 and 22 recites that the human monoclonal antibody binds to a consensus sequence on CD147 comprising RVRS(H). Although the specification on pages 37, lines 9-24 and page 77, lines 22-35 discloses a 15-mer peptide to assay for antibody binding, yet claim a human antibody that binds to a consensus sequence on CD147 comprising a 4-mer or 5-mer peptide. The term "comprising" is an open-ended, it means that a peptide may include additional unspecified amino acids on either or both of the N- or C- termini of a given consensus sequence.

Claim 10 recites that the claimed anti-CD147 human monoclonal antibody cross reacts with hn-RNP-k protein, however, besides SEQ ID NO: 17 disclosed in the specification on pages 38-39, the specification does not provide sufficient guidance and direction as to how to make and to use any heterogenouse ribonuclear protein k (hn-RNP-k protein). The claims as written read on a genus of such proteins. The specification fails to provide guidance on how to make said genus or protein.

Claims 60 and 61 only require either the heavy or light chain amino acid of the human monoclonal antibody that binds CD147. It is well established in the art that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs which provide the majority of the contact residues for the binding of the antibody to its target epitope. The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity which is characteristic of the parent immunoglobulin. It is expected that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites. Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff et al (Proc Natl Acad Sci USA 1982 Vol 79 page 1979). Rudikoff et al. teach that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function. It is unlikely that human monoclonal antibody as defined by the claims which may contain either heavy or light chain variable regions of an CD147 antibodies have the required binding function. Undue experimentation would be required to produce the invention commensurate with the scope of the claims. Further, the specification does not disclose that a functional human antibody can be obtained with either the heavy or light chain. It is noted that the specification does not provide a light chain amino acid for IgG antibody sequences from 2.3.2 antibody (see Fig. 32).

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

19. Claim 10 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of an isolated human monoclonal antibody having an isotype that fixes complement and a variable region that binds the epitope of SEQ ID NO: 1 (ITLRVRSH) on CD147 bound by the IgM monoclonal antibody ABX-ABL; a kit thereof, a pharmaceutical composition thereof and an article of manufacture thereof for the treatment of GVHD, and a human monoclonal antibody that binds to CD147 wherein the heavy chain and the light chain are 23 and 24, 25 and 26, 27 and 28, 29 and 30, 31 and 32, 33 and 34, 35 and 36, 37 and 38, 40 and 41.

Applicant is not in possession of an isolated human monoclonal antibody having an isotype that fixes complement and a variable region that binds to the epitope on CD147 bound by the IgM monoclonal antibody ABX-CBL, "with the proviso that the antibody is not CBL1 (ATTCC HB 8214)" in claims 1, 7, 10, 22 , wherein the isotype is selected from the group consisting of "murine IgM, Murine IgG2a, murine IgG2b, murine IgG3" in claims 4, 6, 9, 10(c), cross-reacts with "hn-RNP-K protein", binds to a "consensus sequence on the CD147 comprising RVRS" in claim 10(e-f) or "to an epitope on CD147 comprising the consensus sequence RVRSH" in claim 22, a kit or an article of manufacture for the treatment of diseases having an etiology characterized by a "harmful presence of activated T cells, B cells, or monocytes" comprising a liquid preparation comprising an amount of an anti-CD147 antibody in pharmaceutically acceptable carrier and instructions on administering said preparation to a patient "suffering from any disease" "having the etiology characterized by a harmful presence of activated T cells, B cells, or monocytes" in claims 27, 31, 35, 38, or a human monoclonal antibody that binds to CD147 wherein the heavy chain has an amino acid sequence of SEQ ID NO: 23, 25, 27, 29, 31, 33, 35, 37, 39 and 40 in claim 60, or the light chain of SEQ ID NOs: 24, 26, 28, 30, 32, 34, 36, 38, and 41 in claim 61.

Neither the exemplary embodiments nor the specification's general method appears to describe structural features, in structural terms, that are common to the genus. That is, the specification provides neither a representative number of species (hn-RNP-K protein) to describe the claimed genus, nor does it provide a description of structural features that are common to species (hn-RNP-K protein). The specification provides no structural description of hn-RNP-K protein; in essence, the specification simply directs those skilled in the art to go figure out for themselves

what the claimed hn-RNP-K protein looks like. The specification's disclosure is inadequate to describe the claimed genus of hn-RNP-K protein.

Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

20. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e2) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

21. Claims 51-52 are rejected under 35 U.S.C. 102(e2) as being anticipated by US. Pat. No. 5,643,740 (IDS ref.).

The US `740 patent teaches the use of an IgM antibody recognizing the epitope recognized by the CBL1 monoclonal antibody secreted by the hybridomal having accession No. ATCC HB 8214 in animal and human studies (see col., 12, under section D and E in particular), wherein the CBL1 was given at 5mg per day for 10 days i.v. (composition) (see col, 13, lines 22-26). Further the `740 patent teaches the dose of CBL1 ascites was 0.5 ml daily for 9 days in 100-200 ml of saline administered intravenously (composition). Given the average human weight is 65Kg, then 5mg/65kg will be about 0.1 mg/kg.

The reference teachings anticipate the claimed invention.

22. Claim 25 is rejected under 35 U.S.C. 102(e2) as being anticipated by US. Pat. No. 6,703,362.

The US `362 patent teaches a method of producing an antibody that binds to the GIT transport receptor binding peptide RVRS (patented SEQ ID NO: 263) comprising the steps of immunizing an animal with the peptide and collecting the antibody (see col., 19, and 20 under section 5.4, patented SEQ ID NO: 263, in particular).

The reference teachings anticipate the claimed invention.

23. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

24. Claims 1-2, 4, 6-7, 9-10, 22 and 25-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over US. Pat. No. 5,643,740 (IDS ref.) in view of US. Pat. No. 5,777,074 (IDS ref).

The `740 patent teaches generating monoclonal antibodies, including IgM antibodies that bind the same epitope/specificity as the CBL1 antibody of the claimed invention as well as their characterization and use for medicinal purposes (see patented claim 1, Col., 1, lines 60-64 in particular). Although the reference does not disclose that the CBL1-specific antigen/epitope as CD147 per se as well as some of the other properties (e.g. cross-reacts with hn-RNP-k, RXRS,

substantially non-toxic to cells expressing CD55 and CD59) of the claimed antibodies/methods; given the properties of the CBL1-specific antibodies, including its reactivity properties against normal and malignant cells and functional properties set forth in columns 9-14, the claimed functional limitations would be expected properties of the referenced CBL1-specific antibodies and methods to make antibodies that recognize the epitope recognized by the CBL1 monoclonal antibody. Further, the `740 patent teaches that the subject antibodies can be used directly as therapeutic agents. For such use, it is desirable to employ antibodies of class IgM, or IgG3 which activate the host's own complement system to reduce the population of activated lymphocytes (see col., 5, lines 30-35 in particular).

The claimed invention differs from the reference teachings only by the recitation of human monoclonal antibody in claim 1-2, 4, 6, 7, 9-10, 22, 25 and 26, a consensus sequence on CD147 comprising RVRS (SEQ ID NO: 106) in claim 10 or RVRSH (SEQ I DNO: 107) in claim 22.

The US `074 patent teaches a method of production of human monoclonal antibody, the identification of the epitope (peptide) to which the antibody binds and the delineation of the biologically important function of the defined epitope are achieved and described in detail by the following out lined immunochemical methods and biological assays (see col., 2, lines 53-59 in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to identify the epitope (peptide) to which the CBL1 antibody binds and make human monoclonal antibody that binds to the epitope on CD147 bound by the IgM monoclonal antibody ABX-CBL using the methods of production of human monoclonal antibodies taught by the `074 patent.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the `740 patent provides sufficient motivation and expectation of success in derive various antibodies of various isotypes to the CBL1 specificity including antibodies for diagnostic and medicinal purposes, including those associated with cancer (e.g. leukemias) and activated T cells (e.g. transplant, autoimmunity).

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

25. Claims 27-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over US. 5,643,740 in view of US Pat. No. 6,291,196.

The teachings of US `740 patent have been discussed, supra.

The claimed invention differs from the reference teachings only by the recitation of a kit in claims 27-30, 35-37, 41-43 and 47; an article of manufacture in claims 31-34, 38-40, 44-46 and 49-50 and instructions for the administration of the antibody in claims 26, 33, 36, 39, 43, 46, 48 and 50.

The US `196 patent teaches that the subject compositions can be provided as kits. The kits include an antibody or an antibody fragment which binds specifically to an epitope on melanoma or prostatic tumor cells, particularly an antibody produced by hybridoma cell line 12f3.2. and means for detecting binding of the antibody to its epitope on melanoma or prostatic tumor cells, either as concentrates (including lyophilized compositions), which may be further diluted prior to use or at the concentration of use, where the vials may include one or more dosages. Conveniently, where the kits are intended for in vivo use, single dosages may be provided in sterilized containers, having the desired amount and concentration of agents (instructions to use). The containers provide the formulation for direct use (see col., 11, lines 21-35 in particular). Further, it is noted that the written material in the instructions is not considered to be within the statutory classes and does not carry patentable weight. See MPEP 706.03(a). Finally, it is a well known convention in the art to place these components in a container for convenience and economy.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to include the anti-CD147 monoclonal antibody designated ABX-CBL in a kit format/an article of manufacture for the convenience and economy of the user. One would have been motivated to assemble the antibody in a kit format for convenient.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

26. No claim is allowed.

27. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Maher Haddad

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600